AMENDMENT

In the Specification:

Page 6, Paragraph 3

C1 The proteins that may be synthesized and delivered by the method of the present invention include, but are not limited to, an antibody, an enzyme, a cofactor, an interferon, a hormone, and a peptide. Furthermore, the proteins include natural proteins, fusion proteins, and mutated proteins.

Page 6, Paragraph 8

C2 Another object of the present invention is to use a hemoglobin promoter to achieve the control of the expression and synthesis of proteins in the precursors of the red blood cells. In addition, another object is to use the strength of the hemoglobin promoter to promote efficiency of the protein synthesis.

Page 10, Paragraph 3

C3 Using the method of the present invention, a protein is produced by the progenitor cells of the red blood cells, and carried by the red blood cells for delivery. Once the red blood cells that carry the protein release into the peripheral blood, the red blood cells themselves have no ability to further express protein. The red blood cells are the temporary storage sites for the protein until the protein is released out when the red blood cells rupture. This is a major distinction between red blood cells and other nucleated blood cells. The latter is capable of protein expression in the peripheral blood.

Page 10, Paragraph 4 which continues on Page 11

Second, the red blood cells provide a natural protection to the protein against degradation. The protein is only contained in the red blood cells because the hemoglobin promoter is active only in the progenitor cells of the red blood cells. Red blood cells do not have a nucleus. Hence, the produced protein will not be degraded by nuclear enzymes. Compared to other nucleated cells, such as white blood cells, the protein will be more stable in the red blood cells. An example of the protein stability in the red blood cells is demonstrated by natural hemoglobin through the life cycle of red blood cells. In addition, the red blood cells also protect the proteins from extra-cellular environment before the proteins enter into the blood circulation.

Page 11, Paragraph 2

Third, the method of the present invention provides an efficient protein delivery mechanism. Natural red blood cells have a half life about 60 days in peripheral blood. Therefore, by utilizing red blood cell rupture as the delivery mechanism the protein supply will be continuous and constant. For certain diseases, for instance, haemophilia and hormone related diseases, continuous protein supply is desired. For other diseases, such as cancer, a constant protein supply not only provide a treatment, but may also contribute to the prevention of the disease. Furthermore, in some cases although a constant protein supply may not be the mode of natural supply, it could be therapeutic and beneficial. A suitable example of such case is insulin supply of diabetes patients.

Page 12, Paragraph 1

Fifth, with the method of the present invention, the amount of protein production and delivery can be controlled by the amount of host cells collected and treated. When the stem cells are collected from bone marrow, the treated bone marrow can be implanted at the original collection position, or enclosed in a bag, then implanted back into a patient's bone marrow. If a large quantity of protein is needed, such as human serum albumin, the amount of protein production can be controlled by the numbers of

transplant sites. If a patient inherits a genetic defect and needs a continuing supply of the normal gene product throughout life, a permanent implantation could be selected. If only short term activity of a gene is needed, such as to activate the immune system against cancer cells or an infectious agent, the bag can be taken out from the body when the therapy is complete, or no longer desired.

Page 13, Paragraph 1

The method of the present invention has a broad spectrum of applications, particularly suitable for gene augmentation therapy, in which a healthy gene replaces the product of a missing or defective gene but does not physically replace the flawed DNA itself. An example of gene therapy using the method of the present invention is to treat a haemophilia patient. In this case, a retroviral vector will be constructed with a hemoglobin promoter and haemophilia factor XIII gene. Then, an amount of bone marrow is collected from the patient and the stem cells is transduced with the vector. The vector construction and gene transduction can be accomplished using procedures known in the art. The bone marrow after treatment then is transplanted back into the patient. After transplantation, the transduced stem cells will produce blood cells. The haemophilia factor XIII will be produced only in the red blood cells which will circulate in the peripheral blood of the patient under treatment. At the end of life cycle of these red blood cells, haemophilia factor XIII will be released into bloodstream upon the rupture of the red blood cells. Because of a continuous generation of red blood cells by the transduced stem cells and continual red blood cell rupture at the end of their life cycle, the patient under such therapy will have continuous supply of haemophilia factor XIII.

In the Claims:

Please delete Claims 9 and 22-23, without prejudice.

Please amend Claims 1, 10, 13-16, 24 and 27-29 to:

1. A method for producing and delivering protein in vivo comprising the steps of:

(a) inserting into a vector a promoter which is active only in progenitor cells of red blood cells, and a gene encoding a protein which is non-native to red blood cells, wherein said promoter and said gene are operably linked;

C8 (b) collecting an amount of progenitor cells of red blood cells from a mammal;

(c) transfecting said progenitor cells of red blood cells in vitro with said vector containing said promoter and said gene;

(d) introducing the transfected progenitor cells of red blood cells back to said mammal, wherein the transfected progenitor cells of red blood cells produce altered red blood cells containing said protein which is non-native to red blood cells in vivo in said mammal, and wherein said protein which is non-native to red blood cells is contained only in said altered red blood cells, and thereafter said protein which is non-native to red blood cells is released into blood stream of said mammal through rupture of said altered red blood cells.

C9 10. The method of Claim 1 wherein the rupture of said altered red blood cells in vivo is induced by genetic mutation, wherein the lifetime of said altered red blood cells is modified.

C10 13. The method of either one of Claims 11 or 12 wherein said protein which is non-native to red blood cells is a naturally occurring protein.

C11 14. The method of either one of Claims 11 or 12 wherein said protein which is non-native to red blood cells is a fusion protein.

15. The method of either one of Claims 11 or 12 wherein said protein which is non-native to red blood cells is a mutated protein.

C12 16. A method for producing and delivering protein in vivo comprising the steps of:

(a) inserting into a vector a hemoglobin promoter and a gene encoding a non-hemoglobin protein; wherein said promoter and said gene are operably linked;

(b) collecting an amount of host progenitor cells of red blood cells from a mammal;

(c) transfecting the host cells in vitro with said vector containing said hemoglobin promoter and said gene;

C12 cont'd

(d) introducing the transfected host cells back to said mammal, wherein the transfected host cells produce altered red blood cells containing said non-hemoglobin protein in vivo in said mammal, and wherein said non-hemoglobin protein is contained only in said altered red blood cells, and thereafter said non-hemoglobin protein is released into blood stream of said mammal through rupture of said altered red blood cells.

C13 24. The method of Claim 23 wherein the rupture of said altered red blood cells in vivo is induced by genetic mutation, wherein the lifetime of said altered red blood cells is modified.

C14 27. The method of either one of Claims 25 or 25 wherein said non-hemoglobin protein is a naturally occurring protein.

C15 28. The method of either one of Claims 25 or 26 wherein said non-hemoglobin protein is a fusion protein.